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The Clinical Use of Radioactive Iodine for the Hyperactive Thyroid: Radioactive iodine atoms emit beta and gamma rays. Two radioactive isotopes of iodine are suitable for attempting treatment for hyperactive thyroid tissue, I^{130}, with a half hife of 12.6 hours, and I^{131}, with a half life of 8 days. The latter was not readily produced until recently, but the former became available in a few localities about 1943, and two groups in Boston employed it for therapeutic purposes in toxic goiter.

Since the release of isotopes from the atomic energy pile at Oak Ridge, Tenn., it has been possible for suitably equipped institutions to obtain I^{131}. Accordingly an appraisal of the treatment of toxic goiter with this agent has been undertaken in several hospitals. The study here reported was begun in October 1946; the material is presented as a preliminary report.

At the start of the work no adequate basis for dosage planning was available. Decision as to the amount of material to be administered involved taking into account the degree of uptake of the radioactive material by the thyroid gland, and its subsequent release therefrom, as well as of the amount of energy released by the radioactive atoms. Calculations were made as follows:

According to theoretical considerations, if a relatively small organ has a uniform concentration of 1 microcurie of I^{131} per gram, and the isotope remains there for total decay, the tissue will receive a radiation dose of about 160 equivalent roentgens. In the case of the toxic thyroid gland, the iodine gradually leaves the organ at such a rate that the effective dose is reduced to about 120 e.r.

Based upon the reports, it appears that patients who were successfully treated with I^{130} received about from 2000 to 4000 e.r. When radiation is delivered more slowly, as with the 8-day isotope, a larger total number of roentgens is necessary to produce the same therapeutic result. Accordingly, in the present series a dose of from 3000 to 5000 e.r. was made the objective. Assuming a 60-gram thyroid, an uptake of 50 percent of the administered material, and a gradual loss by elimination from the gland, a dose of about 4 millicuries would be required to deliver this radiation. Treatments were therefore started with this as the amount administered in all cases, although, because of differences in gland size and in iodine uptake, there would be considerable variation in the actual irradiation administered. Thus, an appraisal of clinical response to various doses would be made. This was desirable, since it was not certain whether the calculated dose of radiation was optimal, or whether it should be more or less.

Radioactive iodine was obtained from the atomic energy pile at Oak Ridge, Tenn. After proper standardization and dilution, the material was given by mouth, in water solution, the iodine being carrier-free (i.e., all of it radioactive). Thus the therapeutic dose of 4 mc. contained only about 0.03 micrograms of iodine, which is well below the normal daily intake of the element. In the early cases a tracer dose was not always given in advance of therapy; later this became routine, in order to obtain information about the uptake.

In addition to the therapeutic administration of the material, numerous tracer studies have been made, to determine radioiodine uptake by individuals with normal and diseased thyroid glands. Tracer doses were usually of the order of from 50 to 75 microcuries; the radiation effect on the gland from this amount is considered insignificant.

When used in therapy and in tracer studies, the radioiodine uptake by the gland was measured at different times after ingestion. The patient was placed on a frame so that the skin over the isthmus of the thyroid was always at 15 cm. distance from the Geiger counter. The first patients were studied from the instant of administration; uptake was followed minute by minute for the first hour, then at 3, 6, 24, and 48 hours. In all cases measurements were made at 24 hours after therapy and weekly thereafter as long as practicable.

Most of the iodine which is not concentrated in the thyroid gland is excreted in the urine, within the first 24 hours. Accordingly, urinary iodine output was followed for 24 or 48 hours whenever possible.

The size of the gland was estimated immediately prior to treatment. To aid in this, a series of plasticine models was constructed and their volumes determined by liquid displacement. They were, for the normal gland, 25 c.c., and for the four stages of enlargement, 35, 50, 70, and 100 c.c. By palpation it was possible to assign a particular patient's gland to one of these groups, or to a value halfway between two. It is realized that this method is inaccurate, but an approximate knowledge of gland size is essential in evaluating this type of therapy. This lack of accuracy must be kept in mind in connection with any statement regarding dosage.

Radiation dosage was calculated for all treatments according to a formula taking account of millicuries administered, percentage uptake, rate of elimination from the gland, and gland size.

Tracer studies were made on (1) persons whose thyroid was normal, (2) persons whose thyroid was hypoactive, and (3) persons whose thyroid was hyperactive. The uptake at 24 hours in the normals varied within the relatively narrow range of from 15 to 30 percent of the administered amount. In hypothyroidism it was under 10 percent, and in toxic goiter it was over 40 percent. The border regions of from 10 to 15 and from 30 to 40 percent appear indeterminate. Administration of stable iodine or of antithyroid drugs within two weeks prior to the test may vitiate the results.

Urinary excretion in the first 24 hours after radioiodine administration varied from 40 to 70 percent in the normals and from 10 to 40 percent in those with hyperthyroidism. The thyrotoxic persons excreted more of the material in the first 6 hours than in the following 18, probably due to increased renal clearance. In the normals, considerably less appeared in the urine in the first 6 hours than in the remaining 18. Thus the measurement of urinary excretion gives an indication of toxicity, although it is not as reliable as measurement of gland uptake.

Up to the present time 40 patients with unquestioned toxic goiter, given 47 treatments with I^{131}, have been followed long enough to permit some evaluation of the results of therapy. The follow-up period has ranged from 4 months to more than a year. Fourteen of the patients were men, 26 women. Ages ranged from 23 to 57. Eighteen of the cases were primary toxic goiter in which there had been no previous treatment of any type, whereas 22 were recurrent after operation and in which antithyroid drug therapy had been administered for some time without satisfactory relief. All but one patient had toxic diffuse goiter; no patient with true hyperophthalmic goiter was treated.

All patients in this series received from 3 to 4 mc. In the 40 patients treated, there were 13 failures after a single dose of I^{131}. Those in whom failure resulted were given second treatments. Six of these were treated too recently for inclusion in this report. Of the other 7 followed for 4 months or more, success was obtained in 3. Four instances of transient hypothyroidism occurred following radioiodine therapy, but gland activity returned to normal within a short time.

With a relatively constant amount of radioactive material, it is obvious that the larger glands collect much less radioiodine per gram of tissue, and hence receive less actual radiation than the smaller. Therefore, as stated above, estimate of gland size is essential, even though admittedly not accurate, to permit calculation of radiation dosage. The number of microcuries administered per estimated gram of gland tissue is related to the result of treatment. With doses of 100 or more μc. per gram, only 2 of 15 patients failed to respond satisfactorily. With lower doses the successes and failures were equally divided.

The actual irradiation of the gland is the result not simply of the microcuries administered per gram of tissue, but of the microcuries retained there. There were no failures in those instances in which more than 75 μc. were retained per gram. On the other hand, only one patient responded satisfactorily to an initial dose of less than 25 μc. retained per gram.

The actual radiation dose in terms of equivalent roentgens depends not only on the uptake by the gland, but also on the subsequent rate of elimination therefrom. Dosages calculated according to the formula allowing for these factors are shown in the charts on the opposite page. There were only 2 failures in 13 treatments of 6000 e.r. or more. In the range of from 3000 to 6000 e.r., successes and failures were equally distributed. The three successes in the lowest dosage range were repeat treatments after inadequate initial responses. The four instances of transient hypothyroidism occurred with doses of 2900, 6900, 7400, and 8600 e.r.

The factors influencing radiation dosage, as has been stated, are the amount of radioactive material administered, the weight of the thyroid gland, the percentage retained in the gland, and the rate of its release. The pre-treatment

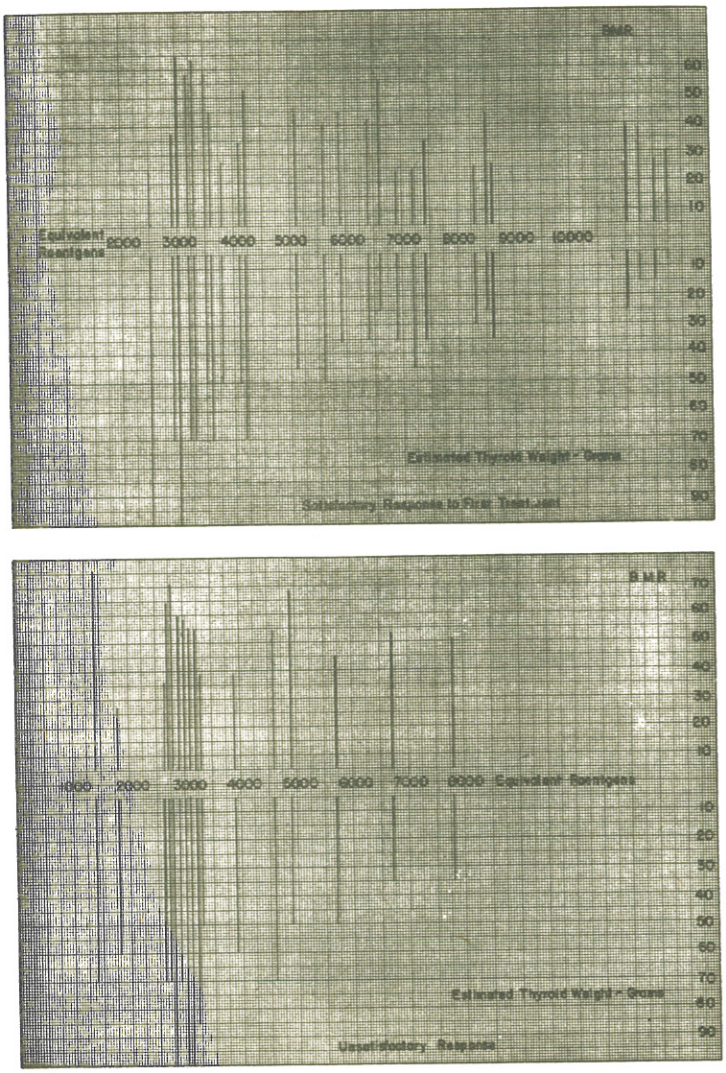

Chart showing radiation dosage, BMR, and gland size for each individual case. Upper part—successful treatment; lower, unsuccessful. Each patient is represented by two lines, starting at the administered dose of equivalent roentgens. The line extending upward indicates the BMR, the one extending downward, the estimated thyroid weight.

level of the basal metabolic rate may also be significant. In an attempt to visualize the importance of some of these factors, the charts are presented to show for each individual case the gland size, pre-treatment BMR, and dose in equivalent roentgens. This dose takes account of uptake and elimination. The upper chart deals with the successful treatments, the lower with the failures.

As would be expected, most of the failures are in the low dosage region, in which are the large glands. The reason for failure in the three or four patients receiving apparently adequate doses is not clear. Possibly the glands were larger than estimated, which would mean that the radiation doses were smaller than indicated. It may be noted that on the whole the failures show higher basal metabolic rates than the successes.

It is interesting to observe that there are a number of successes in the lower dosage region, which, in this series, means large glands. On the average, in the successful cases, there were lower BMR's. There is apparently an actual region of overlap in dosage for successful and unsuccessful therapy. It is important to increase the series and to treat patients with large glands with radiation doses of the same magnitude as those received by patients with the smaller ones.

Although a few successfully treated patients experienced a return in basal metabolic rate to normal in less than 2 months, most of them were not in remission until the end of the second or middle of the third month. A few required even longer.

The incidence of complications resulting from radioiodine therapy is not high. Four instances of transient hypothyroidism occurred with I^{131} doses of from 3

to 4 mc.; these patients received radiation doses of 2900, 6900, 7400, and 8600 e.r. The symptoms and signs of hypothyroidism were noted in the third or fourth months after treatment, and cleared within the space of a month, with one exception, in which the time was somewhat longer. A persistent sensation of a head cold or sore throat occurred in 6 instances with a hacking cough, and in one other, cough alone, without adequate evidence of an upper respiratory infection to account for it. This appeared several weeks after treatment and subsided about a month later. Marked tenderness of the thyroid gland to palpation was noted in 2 cases, subsiding after several months. The glands became indurated; this characteristic was noted in many cases without associated tenderness. Three instances of increased toxicity in the month following therapy were noted. This brought the basal to about 15 percent higher than before therapy, and was sufficient to create alarm concerning the patient's status, though fortunately neither cardiac failure nor thyroid storm was precipitated in any instance. No instance of radiation sickness was noted. Two patients were unwittingly treated in the first 2 months of pregnancy. No apparent harm to patient or fetus has been evident. In most cases the glands were reduced to within normal limits or less by 3 months following therapy, when remission was obtained. In the instances of failure of therapy, gland size was somewhat reduced, although not to normal limits.

Two aspects of radiation hazards must be considered, the danger to the patient and to other individuals. Danger to the patient might be either immediate or late. The analysis of complications just made indicates that there is no immediate danger to the patient from the effects of radiation. The possibility of late radiation damage leading to malignant change cannot be ignored. However, a calculation of radiation dosage administered to many individuals in intensive x-ray therapy of the neck indicates that the hazard with the doses in this series is not great.

A concensus based on experience with x-ray treatment of toxic goiter indicates that later malignant complications from radioiodine therapy are also probably unlikely. (Bull. N. Y. Acad. Med., Sept. '48 - S. C. Werner et al.)

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A New Photographic Material for Gamma-Ray Dosimetry: Photographic methods have been used on a routine basis in the Los Alamos Scientific Laboratory, Los Alamos, New Mexico, for estimating the degree of exposure of personnel to stray gamma and roentgen radiation. Accidents occurring during the handling of fissile materials made it desirable to supplement the standard dental-type roentgen films being used with some other photographic material having the property of being able to record an integrated gamma-ray dose of a higher order of magnitude. Accordingly, a number of commercially available photographic films and papers were investigated in the hope of finding a suitable one. "Adlux" film, manufactured by the Defender Photo Supply Company, was found to be of the desired degree of sensitivity, as well as to possess unusual uniformity and

reproducibility. This film with standard development gives a readable range of densities in the dosage range of from 50 to 15,000 gamma-roentgens.

It became apparent that this range includes the range of dosage of therapeutic interest and that the film should therefore prove useful in the measurement of distribution of radiation intensities about multiple radium sources such as are used in therapy. Such measurements made by means of ionization chamber technics are tedious, while calculations become very laborious or well nigh impossible when more than a few sources or anything but the simplest geometrical arrangements are considered. Film methods have the advantage that a complete three-dimensional plot of radiation intensity about a source or group of sources may be made in a single exposure. In addition, qualitative investigation of the field pattern about a group of sources may be made rapidly and effects of changes in distribution of sources noted. A permanent record is also provided. The degree of precision is not high but is believed adequate for clinical purposes. Film methods in the past have been handicapped to a degree by the limited range of radiation dosage recordable.

The extension of the international roentgen, originally defined for roentgen rays, to the gamma-ray region has been validated by the work of Gray and others. In particular, the conditions under which thimble-chamber measurements are valid as a measurement of dose in terms of the international roentgen have been clarified. The intensity of radiation about a point radium source of 1 millicurie strength and encased in a 0.5 mm. platinum shield, has been determined to be 8.4 r per hour at a distance of 1 centimeter.

Photographic measurements of radiation dose must be calibrated in terms of the primary ionization measurements. There is unfortunately no simple and direct relationship between film blackening and radiation dose. In general, the photographic effect is dependent upon photon energy, the emulsion blackening for unit dose decreasing with increasing photon energy. There are in addition sharp discontinuities in the curve of specific blackening against wave length in the region of the absorption edges of bromine and silver, at 14 and 25 kv., respectively.

The photographic measurement of visible light has been complicated by failure of the reciprocity law of Bunsen and Roscoe, which defines the exposure as equal to the product of intensity by time and implies that equal exposures should result in equal emulsion blackening. It has been shown by Bell, however, that the photographic effect of a given dose is independent of the dosage rate over a range of roentgen-ray intensities varying by a factor of ten thousand. This point has also been investigated by Morgan.

It is customary to plot the characteristic curve of film in the manner suggested by Hurter and Driffield, namely, density as a function of the logarithm of the dose. When this is done an S-shaped curve is obtained which over a considerable portion of the range approximates a straight line. Bell has also shown

that the shape, but not the position, of this curve depends only on the characteristics of the film material and development conditions, and is independent of wave length.

There are many potential sources of error in photographic methods. Uniform development technic with control of temperature and agitation is of utmost importance in obtaining reproducible results. Wilsey has discussed in detail the technical requirements that must be met in photographic methods of measurement of roentgen-ray dose.

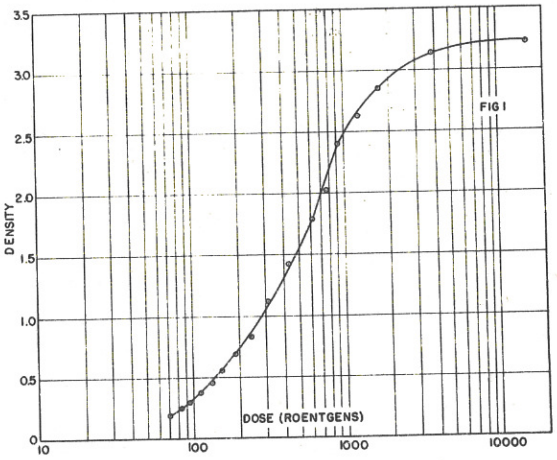
"Adlux" film consists of a transparent safety base double coated with a bromide type of emulsion similar to that used in projection printing papers. A diffusing medium has been added to the film emulsion, which gives it a translucent appearance. The film is designed for the production of advertising display transparencies. The base stock is 0.015 cm. in thickness, and the emulsion layers average about 15 microns in thickness. The grain-aggregate size in the developed film varies between approximately 0.5 and 0.7 microns. The film has a matte surface which has incidentally proved useful through the readiness with which notations and construction lines may be made directly on the film.

Density measurements were made using a "Photovolt" photoelectric densitometer. This instrument incorporates a diffuse illuminating system, phototube and amplifier, with a direct-reading scale calibrated in density units. The primary range of the instrument is from density 0 to 2.0 with provision for extending the range to about 3.2 by resetting the zero point.

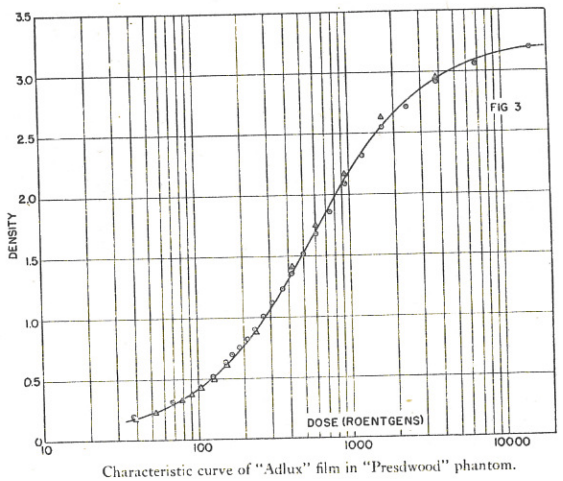
Film exposures were made both in air and in a phantom of Masonite "Presdwood." For exposures in air the film was enclosed in two thicknesses of black protective paper and it and the source were supported on a thin sheet of cellulose acetate at a distance from any dense scattering material. The phantom was made up of 1/4 inch slabs of "Presdwood," and was so arranged that air spaces were avoided, and the film and source were enclosed on all sides by at least 10 cm. of absorbing material. Reference points on the film were located by pin holes punched in the paper packet enclosing it.

The figures on the opposite page give the characteristic response curves of this emulsion material in air and under phantom conditions respectively.

It is surprising to note that this film method shows such close agreement with the inverse square law out to such large distances (approximately 20 cm.) in the phantom. At such distances, differences due to absorption are large and are readily measurable when an ionization chamber is used. The agreement is purely fortuitous and must be due to an increased sensitivity of the film to scattered radiation of longer wave length. However, there is good agreement with



Characteristic curve of "Adlux" film in air.



Characteristic curve of "Adlux" film in "Presdwood" phantom.

ionization chamber measurements out to distances (approximately 10 cm.) which are likely to be of clinical interest.

Investigation of the response of this film to a wide range of photon energies (from 50 kv. to 20 mev.) is under way, and will be reported in the future. Preliminary work indicates that there is no significant difference in the response of the film to the primary radiation of radium, which has an average energy of 0.7 mev., with photon energies ranging from 0.3 to 2.5 mev., on the one hand, and to the gamma radiation from Co^{60} which has well defined photon energies of 1.1 and 1.3 mev.

Gamma-ray dosimetry with the aid of a special, commercially available film has been shown to have unusual latitude and reproducibility. The use of this material for investigation of the radiation field about complex arrays of sources is feasible and the method is capable of giving results well within clinical tolerances of accuracy. (Am. J. Roentgenol., Aug. '48 - H. O. Whipple et al.)

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Hearing Aids: As a result of war discoveries, outstanding advances have been made in the development and use of hearing aids. In evaluating methods for increasing hearing, consideration must be given to the fact that the well-fitted hearing aid can give a gain of from 40 to 50 decibels and that even those with very little hearing can profit from wearing one.

Hearing aids are serving people of all ages from the preschool child to the extremely aged, and from those with a moderate hearing loss of 30 decibels to those who have a loss of 80 or even 90 decibels.

A recent study by Dr. Clarence V. Hudgins of the Harvard research group offers significant data. He tested the responses to spoken words on 26 children

at the Clarke School for the Deaf, first with lip reading alone, then with the hearing aid alone, then with both used together. The average hearing impairment for these children showed a 78-decibel loss. The score for lip reading alone was 43 percent; for a hearing aid alone, 23 percent; when both lip reading and the hearing aid were used, 65 percent. This was in so-called deaf children whose impairment was great and in whose school training lip reading was being emphasized. Patients should be encouraged therefore to use both the hearing aid and lip reading, not either one alone.

It was found in the Harvard studies "that regardless of the nature of their particular defect, most patients hear best with an instrument which amplifies all frequencies uniformly, or with moderate emphasis on the higher frequencies." This is the principle of "high fidelity" as against the commonly accepted principle of "selective amplification" the object of which is to amplify the valleys of the patient's audiogram to make an over-all flat curve as near the normal as possible.

The major specifications which were recommended as a result of the Harvard studies on hearing aids are as follows:

"Frequency Response and Range. Uniform, i.e., without marked resonant peaks or valleys, from 300 to 4,000 c.p.s. Sharp cutoffs below and above this range are desirable. The one best frequency characteristic is a moderate high-tone emphasis of from 4 to 6 db. per octave over this range.

"Tone Control. Preferably by compression amplification; alternatively by simple symmetrical peak clipping.

"Maximum Output. Semipermanent adjustment; or separate models, at 114, 120, 126, or 132 db. re 0.0002 dyne per cm^2. maximum instantaneous acoustic pressure.

"Maximum Acoustic Gain. Separate models would probably be desirable, the lowest powered to have at least 40 db. acoustic gain available, and the highest powered a maximum of 80 db.

"Gain Control. Smoothly graded or in small steps on an approximately logarithmic scale over a 40 db. range.

"Intrinsic Noise. Must not mask speech delivered to the instrument at a sound-pressure level of 30 db."

Hearing aids are being used to advantage in the very young who are deaf to gain better articulation and rhythm in those early years when the child normally learns speech.

The war program has taught the value of auricular training in becoming adjusted to the use of hearing aids.

In the program for civilian hearing aid clinics the Academy of Ophthalmology and Otolaryngology urges that each state have at least one hearing clinic or center where careful otological reviews and tests can be made and a thorough fitting for a hearing aid be made, patterned somewhat after the Army and Navy plan.

Many advances are pointed out in the reports from the engineers of the different companies that manufacture hearing aids. Batteries are of two types, carbon and mercury, and improvements in materials and assembly allow them to be made much smaller and more efficient. This has permitted a drastic change in the size of the transmitter which is now put in a single case. Ethyl cellulose for the case, butyl rubber mountings for insulation, smaller and moisture-proof cords, all make for reductions in clothing-rub noises that so trouble the user. Even the vent in the plastic case has been adjusted to stop further these friction noises. The midget vacuum tubes have been made still smaller, more powerful and free of objectionable resistance noise. The ear receivers are smaller and more efficient. Magnetic receivers have been so improved that many manufacturers use the crystal diaphragm only in the transmitter. One firm has found what it considers a more efficient magnetic diaphragm for the transmitter as well. Plastics for making ear molds are so improved that the agents for hearing aids can safely make them, provided any obstructing wax has first been removed. Elaborate devices are being designed to assist in the selective fitting of the hearing aid. These will be simplified and made more efficient as the significance of the Harvard studies are better understood. Another war product is the printed circuit which is being adapted to use in the hearing aid. It will save much skilled labor in small part assembly, and makes for ruggedness, protection against moisture, and simplicity. Some manufacturers are using the printed circuit with enthusiasm, while others are waiting for electronic engineers in cooperation with the Bureau of Standards to correct the few faults they believe persist. (Ann. Otol., Rhin., and Laryng., June '48 - G. Berry)

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Re Treatment of Pregnant Syphilitic Women During Every Pregnancy: The prevention of prenatal syphilis by treatment of the infected mother during pregnancy is one of the major public health triumphs of medicine. The results in terms of normal living infants, already fairly satisfactory through treatment with arsenic and bismuth, have been still further improved upon by penicillin, which is spectacularly almost completely successful in the protection of the fetus.

Whether or not it has been necessary to treat a syphilitic woman during every pregnancy has been a problem that has troubled all workers in this field. The literature in this country and abroad contains the repeated recommendation that the syphilitic mother should be given "adequate" treatment in every pregnancy, with only a few guarded suggestions that a less conservative policy might eventually be adopted.

Because of the individual and public health importance of the problem, a planned study was cautiously undertaken in 1939 in the Family Syphilis Clinic of the Johns Hopkins Hospital. Three hundred sixty-three selected mothers, treated for syphilis with arsenic and bismuth before or during a previous pregnancy, were deliberately allowed to go through one or more subsequent pregnancies, totalling altogether 570, without additional treatment. Twenty-two women, all of whom were originally treated with penicillin for early syphilis, were observed through twenty-six subsequent pregnancies in which further antisyphilitic treatment was purposely omitted. The infants born of these 596 later pregnancies were carefully followed and studied to determine the presence or absence of syphilitic infection in them.

Of the 597 infants born of these pregnancies during which the mothers were untreated, 549 (92 percent) were born alive.

Twenty of the forty-eight infants stillborn or miscarried were examined at necropsy and evidence of syphilis was found in none.

Of the 549 infants born alive, 88 percent have been carefully followed for more than two months; more than 70 percent for more than one year. All of the children followed are normal and nonsyphilitic.

These data indicate that it is not necessary to administer antisyphilitic treatment to a syphilitic woman during every pregnancy; and that there is a high degree of probability that the infant will be normal if maternal treatment is withheld: (a) regardless of the stage and duration of syphilitic infection in the mother at the time of her original diagnosis and treatment; and (b) regardless of the interval between the previous treatment and the pregnancy in which it is contemplated that further treatment be omitted; provided that (c) the mother has previously received 4.0 Gm. or more of arsphenamine (or its arsenical equivalent) together with bismuth concomitantly; or 2.4 or more million units of penicillin (given for early syphilis in herself; this probably holds good for a maternal diagnosis of late latent syphilis as well); and whether this previous treatment was administered during a previous pregnancy or during a nonpregnant interval; that (d) the mother shows no clinical signs of active syphilitic infection; and that (e) the blood serum of the mother shows a negative test for syphilis, or, if still seropositive, in low titer only (from 1 to 8 dilution units).

Until further information accumulates, a syphilitic woman should be further treated in any pregnancy in which she herself shows clinical evidence of active syphilitic infection; or in which, in the absence of such clinical evidence, she herself has a positive blood STS in a quantitative titer of 16 or more dilution units. (Am. J. Syph., Gonor. & Ven. Dis., Sept. '48 - M. S. Goodwin and M. S. Farber)

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The Role of High Blood Penicillin Levels Achieved with Caronamide in Penetrating the Blood-Brain Barrier: In a previous report the authors described a method for producing sustained high penicillin levels in the blood. This consisted of frequent, rapid intravenous injections of large doses of crystalline penicillin in conjunction with the oral administration of caronamide (4 -carboxyphenylmethanesulfonanilide). The latter inhibits tubular excretion of the antibiotic. The method was found to be safe and effective.

In a review of previous investigations, Wyke reported disagreement on the question of whether any penicillin traverses the blood-brain barrier under normal and abnormal conditions. When penetration into the spinal fluid was reported the levels recorded were low. Smith and collaborators gave 100,000 units of penicillin intravenously to patients with normal and inflamed meninges and found only traces of penicillin in the spinal fluid. They concluded that the meninges are relatively impermeable to penicillin. Schwemlein and co-workers administered penicillin by intravenous drip in amounts varying from 10 to 25 million units in twenty-four hours and found the highest spinal fluid level thus achieved to be 0.55 Oxford units per milliliter. Because of these and similar findings by other workers, patients with cerebrospinal infections have been treated by the intrathecal route, a procedure not without hazard.

For this study, twelve patients free of infection of the central nervous system were selected. In eight of these twelve patients, one million units of crystalline penicillin were administered rapidly intravenously every hour for ten hours. In four, namely, Patients 3, 4, 5, and 7, a continuous intravenous infusion of 10-percent glucose in 1,000 c.c. of distilled water was administered during the ten-hour period, and the penicillin was injected every hour into the distal end of the rubber tubing. Eight patients received caronamide in doses of 4 Gm. every three hours starting eighteen hours prior to and continuing during the period of administration of the antibiotic. These included six patients who received the hourly injections and two who received penicillin along with a continuous intravenous injection of glucose. For comparison caronamide was withheld from the remaining four patients.

The peripheral venous blood and the spinal fluid samples were obtained approximately fifteen minutes after the last (tenth) injection of the penicillin. In some of the patients, specimens also were obtained fifteen minutes after the fifth as well as the tenth injection, and fourteen hours after the last (tenth) injection.

The method of penicillin assay was a broth tube dilution method using Staphylococcus aureus, strain H, as the standard organism and fresh meat extract broth as the medium. The minimal concentration of the standard penicillin required to inhibit the inoculum of 5×10^2 Staph. aureus, strain H, cells was 0.02 units per milliliter. All titrations of blood and spinal fluid levels were accompanied by and compared with this standard.

It may be seen from the table below that substantial penicillin levels were achieved in the cerebrospinal fluid, especially when caronamide was employed

PENICILLIN LEVELS IN THE BLOOD AND CEREBROSPINAL FLUID AFTER THE ADMINISTRATION OF ONE MILLION UNITS OF CRYSTALLINE PENICILLIN EVERY HOUR FOR TEN HOURS, WITH AND WITHOUT CARONAMIDE (IN OXFORD UNITS PER MILLILITER)

	TIME					
	AFTER FIFTH INJECTION		AFTER TENTH INJECTION		14 HOURS LATER	
PATIENT	BLOOD	SPINAL FLUID	BLOOD	SPINAL FLUID	BLOOD	SPINAL FLUID
			With Caronamide			
1	266.0	2.0	160.0	4.4	2.0	0.8
2	260.0	2.0	280.0	6.0	4.4	0.8
3*			100.0	2.0		
4*			140.0	5.0		
5			280.0	1.0		
6			280.0	6.6	20.0	0.08
7			220.0	4.4		
8			300.0	2.5		
			Without Caronamide			
3			40.0	0.24		
5*			12.5	0.133		
7*			40.0	1.0		
9			20.0	0.133		

*Injection made into tubing of continuous intravenous drip.

as an adjuvant. The levels in this group ranged from 1.0 to 6.6 units per milliliter of spinal fluid, with an average of 4.0 units per milliliter. In two patients tested after the fifth injection a level of 2.0 units of penicillin per milliliter of spinal fluid was present. Penicillin was still found in the spinal fluid in the patients tested fourteen hours after the last injection.

In a number of instances the blood penicillin levels were not as elevated as had been anticipated. This occurred in two patients who received the antibiotic via the intravenous tubing through which a 10-percent solution of glucose was being administered. It is believed that loss of penicillin because of diuresis may have played a role. In all the patients who received intermittent injections and caronamide, the blood penicillin levels were markedly elevated as previously reported. Considerably less penicillin was found in the blood and spinal fluid of those patients who did not receive caronamide.

These studies demonstrate that substantial penicillin levels can be attained in the cerebrospinal fluid of patients with normal cerebrospinal systems. These levels are presumably due to the elevated blood levels and not to a change in permeability of the meninges. However, it is possible that even higher levels might be attained in the presence of diseased and more permeable membranes. In such cases intrathecal administration of penicillin in the treatment of the infections might prove unnecessary. (J. Lab. and Clin. Med., Aug. '48 - H. D. Janowitz et al.)

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Effectiveness of Vitamin B12 in PA with Evidence of Nervous System Lesions: In a patient with pernicious anemia in relapse and showing marked neurological

manifestations that developed during irregular treatment with synthetic pteroylglutamic acid (folic acid), a hematologic remission and rapid and marked improvement in the symptoms referable to involvement of the nervous system followed treatment with crystalline vitamin B_{12}. The patient showed severe local and systemic sensitivity reactions to purified liver extracts derived from both pork and beef, but not to vitamin B_{12}.

The findings in this patient whose case history is fully reported by the authors suggest that vitamin B_{12}, like the presently available injectable liver extracts, should prove effective against the neurologic as well as the hematologic manifestations of pernicious anemia. They also suggest that vitamin B_{12} is not responsible for sensitivity reactions to liver extracts. (New England J. Med., 26 Aug. '48 - L. Berk et al.)

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The Effect of Liver Extract and Vitamin B_{12} on the Mucous Membrane Lesions of Macrocytic Anemia: The authors, Robert E. Stone and Tom D. Spies, state that for more than twenty years they have been studying the mucous membrane lesions of persons with macrocytic anemia and have observed that they usually are relieved by liver extract and ventriculin. A great opportunity to study more carefully the pathogenesis of these lesions appeared with the advent of pteroylglutamic acid (folic acid) in 1945 and 5-methyl uracil (thymine) in 1946, two pure chemical compounds which are effective in producing a hematologic response in certain types of macrocytic anemia.

As soon as it had been demonstrated that synthetic folic acid and synthetic thymine were effective in producing a hemopoietic and clinical response in persons with pernicious anemia and related anemias, additional studies on these substances were planned. These studies were directed toward answering the following questions: What clinical syndromes are affected by these chemical compounds? What is the relation of the structure of the molecule of these compounds to their antianemic properties? What are the relative clinical and hematologic effects of these substances as contrasted with each other and as contrasted with liver extract? How well do these substances maintain patients with pernicious anemia, nutritional macrocytic anemia, and tropical sprue? As a partial answer to this last query, the authors (and many others), during the past two and one-half years, have found that folic acid maintains the blood levels in persons with pernicious anemia just as well as liver extract but that it does not offer a complete treatment in most cases because it does not prevent or relieve subacute combined degeneration of the spinal cord. It appears from their studies that folic acid is preferable to liver extract in the maintenance of persons with nutritional macrocytic anemia and tropical sprue. They have found that thymine, like folic acid, is not a complete treatment in most cases of pernicious anemia for it neither prevents nor relieves the subacute combined degeneration of the spinal cord, although it does maintain the blood levels very well. Unpublished observations show that massive doses of thymine are as effective as liver extract

or folic acid, both clinically and hematologically, in maintaining persons with nutritional macrocytic anemia and tropical sprue. The very large dose required, however, makes thymine impractical as a therapeutic agent.

In two and one half years of study, the administration of either folic acid or thymine did not result in healing the very severe mucous membrane lesions in cases of pernicious anemia. In every instance the administration of liver extract was followed by prompt improvement. This improvement lasted for varying degrees of time after the cessation of liver extract therapy. The earliest relapse occurred one month after therapy was discontinued, and several patients had had no recurrences twelve months after therapy was discontinued. The great majority had a recurrence from within one to nine months after the last injection.

Three of the patients were uncooperative and, feeling very much better, would return to work and not wish treatment again. When they relapsed, they returned. These three patients had, at intervals, treatment with massive doses of thymine, parenteral liver extract, and orally administered folic acid. In addition two of them had treatment with vitamin B_{12}, the newest vitamin to be isolated and found to be effective in producing a clinical and hematologic response in persons with Addisonian pernicious anemia, nutritional macrocytic anemia, and tropical sprue. The fiery redness and intense pain of the mucous membrane lesions were relieved, at least temporarily, in these two patients.

These studies show that certain patients with Addisonian pernicious anemia have severe mucous membrane lesions that are not relieved by the administration of massive doses of thymine or large doses of folic acid. These severe mucous membrane lesions are characterized by a fiery red appearance and, in most instances, excruciating pain to the patients. These severe lesions have been seen only in patients with pernicious anemia, that is to say, patients who had gastric achlorhydria and achylia, and in each instance these lesions have occurred only in people who had subacute combined degeneration of the spinal cord. There seems to be a close clinical association between the gastric defect, the severe mucous membrane lesions, and the degeneration of the posterior and lateral columns of the spinal cord in these particular patients.

Without exception, in the experience of the authors, the patients, as illustrated by the case history which they report as representative of the various ones in this study, have benefited from liver extract injections, and two of them were given vitamin B_{12} with similar relief for at least two weeks' time. These findings support the authors' previous contention that neither thymine nor folic acid is a complete treatment for persons with pernicious anemia, whereas, in contrast, parenterally administered liver extract is. (J. Lab. and Clin. Med., Aug. '48 - R. E. Stone and T. D. Spies)

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New Pregnancy Test: The new pregnancy test that the author devised was suggested by results obtained with estrone in treatment in amenorrhea. It consists

of three intramuscular injections of 1 mg. of estrone in 1 c.c. of oil, given over a period of five days in selected patients. Failure to menstruate within twenty-four hours after the last injection is interpreted as a positive test for pregnancy. The result is sometimes obtained within a few hours, and always within six days. The test has been used with slightly varying technic on some 250 patients without a single incorrect result.

Although the test has proved completely accurate in the author's experience so far, it is expected that many failures will occur, but the percentage of accuracy should still be high.

The following conditions determine the suitability of a patient for this test: (1) she must have a history of reasonably regular menstrual periods; (2) her menstrual period must be overdue (there must be no vaginal bleeding present); (3) she must be fairly healthy in appearance, with no marked anemia to be noted on inspection of the tongue; (4) she must present reasonably normal findings at pelvic examination although she may have signs suggesting pregnancy; (5) she must not have had any recent treatment with other endocrine products (thyroid is a possible exception).

On the patient's first visit a history is taken and a physical examination, including pelvic examination, is made. If she satisfies the five conditions previously stated, she is considered suitable for the test as follows:

1. One mg. estrone in oil is injected deep into a deltoid muscle.
2. Approximately forty-eight or seventy-two hours later a similar injection is made into the other deltoid.
3. Approximately 120 hours (five days) after the first injection, an injection of 1 mg. estrone in oil is administered into the deltoid which was first used, but if this injection cannot be made because the fifth day falls on a Sunday, the second injection is made seventy-two hours after the first, and the third injection is made six days after the first.

If menstruation occurs after the first or second injection, a diagnosis of not pregnant is made and no remaining part of the test is required. If a vaginal flow of blood begins within 24 hours after the third estrone injection and lasts 24 hours or more, the patient is presumed to be not pregnant. If the patient fails to have a vaginal flow, she is presumed to be pregnant. The patient either has what usually appears to be for her a fairly normal menstrual period or she does not flow at all.

Of 50 patients on whom the author had complete data available, the ages varied from 15 to 46 years, 25.6 years being the average and 23 the median. The menses were overdue from 3 to 36 days, with an average of 13 days and a median of 11 days.

There was in each case some reason for performing the test. In some the time overdue was so short that an accurate diagnosis from pelvic examination

alone was unlikely. Several patients were too obese for a satisfactory pelvic examination to be made. Others denied the possibility of pregnancy or insisted on some further assurance that the diagnosis already made clinically was correct. One patient was so near the menopause age that confirmation was desired.

On pelvic examination alone, a correct diagnosis was made in 42 (84 percent) of the 50 patients. An incorrect positive diagnosis was made five times and an incorrect negative diagnosis three times.

Of these 50 women, 19 were shown by the test not to be pregnant; 31 were correctly diagnosed as pregnant. Of the 19 nonpregnant women, 13 (68 percent) menstruated after the first injection of estrone; 4 (21 percent) after the second; and 2 (10 percent) required 3 injections. In the 19 nonpregnant women the shortest time required for bleeding to start after the beginning of the test (first injection) was one and one half hours. The longest time was 134 hours, the average being 44.

The accuracy of the interpretations of the results with this test was determined by careful follow-up. One patient who was pregnant and had had slight spotting had a spontaneous abortion some weeks after the test. Two who were pregnant had resorted to induced abortion. The others who were shown by the test to be pregnant have either been delivered or are well on their way to term. All those in the nonpregnant group have continued with normal menses.

Stilbestrol by mouth was tried as a pregnancy test on one patient without success.

In all of the various 250 patients whom the author has tested for pregnancy there has been no difficulty whatever in interpreting the findings. All of the nonpregnant women had what appeared to be for them a fairly normal menstrual period. In a few of these women the rate of flow was reported as slightly increased, usually with some shortening of the duration of flow.

Practically all in the nonpregnant group were carefully questioned as to the passage of clots or tissue. If a woman was in the habit of passing small clots during menstruation, she usually did the same following administration of the test. One patient stated that this was more noticeable. No one ever stated that she passed large clots or anything resembling tissue.

It used to be thought that the administration of estrogenic substance would produce abortion in humans, but this idea has been disproved by Vaux and Rakoff and by Karnaky. It is possible that it may do so in animals, including monkeys, (Hartman) but in humans, on the contrary, estrogenic substances are now used in the treatment of threatened abortion and habitual abortion.

Those in the pregnant group, as shown by this test, reported no bleeding whatever. The only exception to this was one patient who told of noticing a spot

of blood on her clothing the size of a five cent piece 19 hours after the second injection. This was ignored in interpreting the test, and the third estrone injection was given with no further bleeding noted.

It is possible that menstruation occurring in nonpregnant women receiving the test is in a few cases coincidental; that is, it would have happened without the test treatment. However, it is unlikely that this occurs in many cases because 68 percent of the nonpregnant women menstruated after the first estrone injection while only 10 percent menstruated after the third dose, and all menstruated within 24 hours after the last injection.

The following theoretical explanation for this pregnancy test is based on the results of experiments in monkeys. If it is reasoned that delayed menstruation is due to progesterone secretion that persists because of incomplete degeneration of the corpus luteum, then the antagonistic action of estrone against progesterone eliminates the last effect of the declining progesterone action and allows menstruation to begin.

There is no known proof that delayed menstruation is due to persistence of the corpus luteum although from the results of experiments in animals, it is a likely explanation. Corner's theory of menstruation is based on the cyclic variation of progesterone. It is realized, however, that merely because a certain endocrine action is noted in animals, it does not mean that this action will be the same in women.

Another possible factor in this test is the hyperemia of the uterus and other organs produced by administration of estrogens.

The pregnancy test herein described is applicable to the vast majority of those seeking a diagnosis concerning pregnancy.

The greatest shortcoming of this test is that it is not applicable to a patient who is bleeding.

Because the test has been used only on four women approaching the menopause, caution should be used in the interpretation of results in such patients until more data is available. (Am. J. Surg., Sept. '48 - S. S. Garrett)

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New Factors in Shock and Hypertension: In a series of papers a group of workers from Cornell University Medical College reports the results of its investigations into certain of the problems of shock and hypertension. They have demonstrated the existence of two hitherto unrecognized blood-borne vasotropic substances which they have named vasodepressor material (V.D.M.) and vasoexcitor material (V.E.M.). These substances are assayed by the following technic. A rat mesoappendix is prepared for observation of its vessels;

increasing concentrations of adrenalin are applied locally, and the response of arterioles of a certain size is noted. The concentration of adrenalin needed to induce certain alterations in the circulation is taken as an end point. The material to be tested - e.g., plasma - is now injected into the tail vein of the rat, and the adrenalin sensitivity is re-assayed. They find that this indirect technic based on the response to adrenalin is more reliable than directly observing the alterations in circulation in the mesoappendix that accompany the alterations in sensitivity to adrenalin.

V.D.M. depresses the responsiveness to adrenalin, causes diminished frequency of vasomotion (contraction and relaxation) of the metarterioles and precapillaries, slows capillary circulation, and may cause a fall in blood pressure. V.E.M. has the converse action and stops the circulation in some capillaries.

The blood of animals (rats, rabbits, and dogs) in which shock was induced by tourniquet, leg pounding, Noble-Collip drum, and by hemorrhage showed alterations, which could be repeated, in the blood content of V.E.M. and V.D.M. as shock developed. When the animal was in mild or early shock its blood caused a 10- to 20-fold increase in adrenalin sensitivity on test preparations (V.E.M. activity). Later the adrenalin sensitivity fell to well below that found with control animals, and this rise in V.D.M. activity was associated with the development of irreversible shock which no longer responded permanently to fluid replacement therapy. By assaying extracts of organs of animals killed during various stages of shock it was shown that V.E.M. is produced only by the renal cortex, and that V.D.M. is produced by the liver and to a less extent by the spleen and muscle. The same workers also isolated the substances from these organs when they were incubated under anaerobic conditions. When incubated aerobically kidney destroyed V.E.M. and liver destroyed V.D.M. and to a less extent V.E.M.

Mazur and Shorr have prepared V.D.M. in a partially purified state such that 0.1 gamma can be easily assayed. It is apparently a protein of molecular weight from 10,000 to 15,000, and iron appears to be an essential part of the active molecule. Less is known about V.E.M., but it appears to be distinct from renin or angiotonin. Because of the circulatory change that V.D.M. causes, it seems likely that it plays a part in the development of shock, but, as Chambers and Zweifach themselves point out, so do other factors.

In an extension of this work, Shorr et al. have shown that the kidneys produce V.E.M. under the same circumstances in which they produce renin in experimental Goldblatt hypertension, but there is an important difference in that V.E.M. can be demonstrated in chronic experimental hypertension whereas renin cannot, for it apparently disappears with the acute phase. A curious and as yet unexplained finding is that V.D.M. is also produced in chronic experimental hypertension and masks the V.E.M. activity. To demonstrate the V.E.M. it is necessary to incubate the plasma aerobically with liver to destroy the V.D.M. Of great interest is the finding by this technic that 12 patients with essential hypertension had raised amounts of V.E.M. and V.D.M. in the blood. What part, if any, these

substances play in the genesis of essential hypertension remains to be seen, and this work raises the hope that the actions of V.E.M. may explain much that those of renin have failed to do. (Brit. M. J., 14 Aug. '48 - Annotation)

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A Liquid Adhesive: In 1938 Duo Liquid Adhesive (Johnson & Johnson Co.) was advocated for use in the application of small dressings to wounds of the scalp and face. For this use it was found far superior to adhesive tape and every other adhesive substance which the author had used for making dressings adhere to the scalp and face. It was believed that this liquid adhesive could be used to seal off the hair for cranial operation in patients who did not wish to have their entire head shaved. This liquid adhesive has been used successfully in this manner for over three years.

Duo Liquid Adhesive can be used to seal off the hair for any operation upon the head or face. It is most useful, however, in (1) suboccipital operations, either midline cerebellar exposures or unilateral incisions for fifth and eighth nerve sections, etc.; (2) frontal flaps, unilateral or bilateral where the concealed incision is made just behind the hairline; (3) ventriculogram and other exploratory trephine operations; and (4) prefrontal lobotomies.

The scalp is shaved over the area which is to be exposed for surgery. The hair need be removed only about 1 cm. or so beyond the line of the scalp incision. The liquid adhesive is supplied in a tube and has the appearance and consistency of tooth paste. It is applied about the shaved area, half in the hair and half on the bare scalp. From four to six thicknesses of gauze cut large enough to cover the entire head and hair are placed over the head and the soft paste worked through the gauze by gentle pressure with a blunt object. Only from two to three minutes are necessary for the adhesive paste to dry and the gauze to become firmly adherent to the scalp and hair. With a sharp scissors the gauze over the operative area is cut off. The exposed area of scalp can then be scrubbed for sterile preparation with soap and water, iodine, alcohol or any other liquid (except ether) without fear of dislodging the dressing. The liquid adhesive is a rubberized compound and aqueous or alcoholic solutions do not interfere with its adhesive property. The skin incision is then scratched 1 and 1/2 cm. (or more) inside the gauze edge, draped with sterile wet towels and secured to the scalp with sutures or small towel clips. The towels are then raised and a thin rubber sheet is slipped between them and the gauze. The patient's head and hair as well as the gauze covering it are thus kept clean, dry, and free from blood stains.

At the end of the operation the large gauze dressing covering the hair is not removed but left adhering to the scalp. Sterile dressings are placed over the wound and the entire head bandaged. On the second or third postoperative day, when the skin sutures are removed, the large gauze square may be taken off and the wound covered with a liquid adhesive dressing. The gauze may be

left in place until the wound is completely healed. Upon removing the dressing it will be found that all of the liquid adhesive adheres to the gauze and comes off with it. None is left on the skin or hair to be cleaned off with ether and benzene as is necessary with other adhesive products. (Am. J. Surg., Sept. '48 - R. B. Cloward)

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The Antirheumatic Effect of Sodium Gentisate: The mechanisms involved in the rheumatic diseases are as unknown as is the mechanism in the antirheumatic action of salicylate. Salicylate administration has been shown to inhibit the spreading effect of hyaluronidase. In vitro, however, salicylate inhibits hyaluronidase in very high concentrations only, whereas the biological oxidation product of salicylate, gentisic acid, does so in vitro in concentrations of a few µg. per ml. The inactivation of the enzyme is apparently irreversible and is believed to be due to a condensation of the semiquinone with the enzyme protein.

Because increased hyaluronidase activity has been suspected as a possible cause of the breakdown of interfibrillar cement in rheumatic diseases, the antirheumatic action of Na gentisate (supplied by Hoffmann-LaRoche, Inc., Nutley, New Jersey) has been investigated in a small number of patients. The results have been sufficiently uniform to warrant the present report. Gentisate has the same antirheumatic effect as salicylate, without some of its disadvantages. In 5 patients with acute rheumatic fever, the administration of Na gentisate in doses comparable to those customarily employed for salicylate has been followed by disappearance of pain, swelling, and heat in the joints, by the fall of temperature to normal, and by fall in sedimentation rate. In one patient, withdrawal of gentisate after 3 days of administration was followed within 44 hours by a return of acute joint symptoms, which again responded promptly to the renewed administration of gentisate. The joint pain of 7 patients with rheumatoid arthritis has responded similarly to gentisate and to equivalent amounts of salicylate. In one patient, the salicylate was not tolerated because of the co-existence of a chronic duodenal ulcer, whereas gentisate caused no gastric irritation. Four patients with chronically active rheumatic fever have responded to gentisate and to salicylate similarly.

No untoward effects have been observed in the patients given as much as 10 Gm. per day, except that one patient who, on 8 Gm. per day, developed some epigastric distress which subsided immediately on withdrawal of the gentisate. No significant increase in prothrombin time, and no tinnitus or aural symptoms have developed. No sign of methemoglobinemia or of liver damage has been observed. It seems significant that the increase in urinary glucuronic acid excretion observed with salicylate ingestion does not occur with gentisate.

Only about one quarter of the gentisate ingested was recovered in the urine as gentisic acid. So far the authors have been unable to detect gentisic acid in

the blood, using a color method by which 5 gamma per c.c. of hydroquinone in the urine can be detected. It appears that gentisate is rapidly oxidized in the body.

In summary, sodium gentisate appears to exert antirheumatic activity equal to, or greater than, that of salicylate. It is suggested that the antirheumatic action of salicylate is due to its oxidation product, gentisate. A detailed report of this work will be published shortly. (Science, 10 Sept. '48 - K. Meyer and C. Ragan)

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A Comparative Study of Tellurite-Plating Media for Corynebacterium Diphtheriae: In recent years several new types of media containing potassium tellurite have been recommended for the isolation of Corynebacterium diphtheriae. Few well controlled comparative studies of the merits of these plating media have been published. Because the authors, working in the Department of Bacteriology of the Johns Hopkins School of Hygiene and Public Health, have access to considerable numbers of throat cultures to be examined for diphtheria organisms, they undertook such a study, using the following:

A. Blood-cystine-tellurite agar
B. Mueller tellurite-serum agar
C. Kellogg and Wende tellurite-blood agar
D. Bacto-tellurite agar
E. Trypticase-serum-tellurite agar
F. Bacto-proteose no. 3 agar with potassium tellurite
G. Kellogg and Wende tellurite-blood agar (unheated)

The cystine-tellurite agar (A) was used as a basis for comparison with the others because it has been used in the authors' laboratory for many years and its properties are well known. The other media were selected because they have had a considerable vogue in Europe or North America or both, or because they were described as offering particularly desirable features.

Medium	Letter	Cultures plated	Positive isolations	Per cent positive isolations
Blood C.T.	A	637	100	15.7
Mueller	B	535	69	12.9
Kellogg chocolate	C	634	106	16.7
Kellogg fresh blood	G	203	37	18.2
Bacto-tellurite	D	484	67	13.8
Trypticase	E	520	64	12.3
Proteose no. 3 agar	F	99	12	12.1

The numbers of cultures streaked on each type of medium as well as the numbers and percentages of morphologically positive cultures yielded by each are shown in the table on the left.

The superiority of the fresh blood-containing mixtures (A, C, and G) over the others, both in respect to the size of the colonies of C. diphtheriae and their distinctive dark color, was soon recognized. The dark color of the agar was much easier on the eyes

when large numbers of plates were examined. The colonies on medium C tended to be somewhat larger than those on medium A. Added to the numerical advantage in numbers of positive results obtained, these practical advantages are of great importance.

Two of the most satisfying media, A and C, were streaked with practically the same number of cultures and yielded virtually the same results, 15.7 percent and 16.7 percent, respectively. Medium G streaked with 203 cultures gave the highest percentage of isolation, 18.2 percent. However, if more cultures had been streaked on medium G, especially during the latter part of the study when large numbers of negatives were obtained on all media, the percentage of isolations would have been reduced. The two media containing serum (B and E) were streaked with about the same numbers of cultures; the numbers of isolations were almost identical, both being significantly lower than the numbers yielded by media containing whole blood. The medium containing the laked blood-tellurite solution (D) fell between these two groups. There was no regularity in the capacity of any one medium to rectify failures of any other.

There were some instances of "exclusive" isolations, i.e., in which one medium yielded a positive result when no other did. More exclusive isolations (7 in all) were obtained on medium C than on any other; a total of 12 exclusive isolations were made on A and C.

The data indicate that, for the routine isolation of C. diphtheriae, tellurite media containing whole fresh blood are superior to those containing serum only, or a laked blood-tellurite solution. (Am. J. Hyg., July '48 - M. Frobisher et al.)

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Coloring Acrylic Resin for Anterior Crown and Bridge Restorations: Since the advent of widespread use of plastics in prosthetic dental restorations, exact color matching to insure color harmony with the remaining natural teeth has become the problem of the operator and technician and not of the manufacturer. Since failures are frequently encountered with conventional methods, the following technic is suggested for checking and controlling color blending at the time of test-pressing, instead of at the time of insertion of the finished crown or bridge restoration when it is too late to change shade.

Color selection should be done adjacent to a large window, employing single members of the shade guide moistened with the patient's saliva and with the patient at arm's length. This is the conversational distance at which they are to be viewed; errors can be made if the selections are made from a shorter distance. A bright sunny mid-day north light is best. Whatever over head artificial light there is present is allowed to remain during selection.

All guides should be employed. Much trouble with shades has occurred when the Trubyte New Hue guide is used exclusively because the teeth on this

guide all have translucent incisals, and the dentist is obliged to build a translucent incisal in every case to effect a match. The fact is, however, that many anterior teeth do not have translucent incisal thirds, particularly if they are worn or are backed by gold. Hence all guides should be tried in all cases.

When the most nearly matching shade guide tooth is decided upon, the number is carefully noted as the basic shade. Now two others are selected - the nearest one on the gray side and the one which most nearly matches on the yellow side. These numbers are also carefully noted. Blending is done to match the basic shade when the crown or bridge restoration is being test-pressed. The top half of the flask is placed in hot water for a few moments before pressing, in order to harden the surface slightly and permit making color comparisons in a shorter period of time. When the flask is opened, the color is immediately checked against the basic guide, using a distance and light identical with those employed in making the selections from the mouth. Sometimes, wetting the guide tooth and the cellophane covering the plastic will facilitate color comparison. If the color does not match the basic shade perfectly so far as can be observed, it is modified by additions of further powder and liquid until the technician is satisfied that he has attained the nearest match possible by using only the single basic matching shade guide tooth.

The crown, or bridge restoration, is then pressed again to obtain a glossy surface, and immediately checked against the guide tooth which is just slightly too gray. Because contrast can often be observed more easily than similarity, the same degree of contrast that was noted in the mouth, if present, should be easily discerned. If on the other hand the plastic in the flask seems to match this grayer guide tooth as well as it matches the basic one, the plastic is too gray and more blending must be done until the slight contrast can be recognized.

This procedure is then repeated with the guide which is just slightly too yellow. When the basic shade matches perfectly, with the gray contrast and yellow contrast as noticeable as they were in the mouth, an excellent result is a certainty. (U.S. Nav. Dent. School, Bethesda, Md. - Crown and Bridge Dept.)

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Effect of Resection of Mesenteric Lymph Nodes on Intestinal Fat Absorption in the Dog: A study was made to determine whether intestinal fat absorption may be impaired, and intestinal fat excretion increased by experimental interruption of the mesenteric lymph drainage. It was believed that such experiments might yield data relevant to the question, recently discussed by Frazer, of the extent to which fat absorption may be a function of the portal, as well as of the intestinal, lymphatic circulation. In addition, such experiments might be expected to furnish information on the mechanism of lacteal obstruction, with steatorrhea, which has been described in patients with tuberculous or lymphomatous mesenteric lymphadenitis. Resection of the mesenteric lymph nodes in 10 dogs did not alter fecal fat and nitrogen excretion. In each, there was rapid re-establishment of anatomic and functional continuity of the interrupted mesenteric lymphatics. In 6 animals, partial regeneration of the lymph nodes occurred. Studies were made on plasma lipids in 4 animals, 3 of which showed normal values from 6 to 12 days after operation. (Am. J. Physiol., 1 May '48 - B. G. Clarke et al.)

U. S. Naval Dental Clinic, Guantanamo Bay, Cuba, a Separate Command: The Secretary of the Navy has announced the establishment of the U. S. Naval Dental Clinic, Guantanamo Bay, Cuba, as a separate command. The activity is under the military command and coordination control of the Commander, U. S. Naval Operating Base, Guantanamo Bay, Cuba, and is under the management control of the Bureau of Medicine and Surgery.

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Naval Hospital Dental Services Approved by A.D.A.: The Hospital Dental Service Committee of the American Dental Association announced that the naval hospitals at (1) Annapolis, Maryland, (2) Guam, Marianas Islands, (3) Newport, Rhode Island, (4) Philadelphia, Pennsylvania, and (5) St. Albans, Long Island, New York have met the basic standards required by that committee for approval of hospital dental services.

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Concerning Attendance at a Hospital Corps School as a Requirement for Advancement of Hospital Corpsmen: Recent information has been received from the office of the Chief of Naval Personnel to the effect that due consideration will be given to requests from hospital corpsmen for waiver of the requirements of BuPers Circular Letter No. 74-48. This letter makes Class "A" Hospital Corps School attendance mandatory for eligibility for advancement to petty officer ratings in the Hospital Corps. Men who have sufficient prior service or who have had experience that would be considered equivalent to a Hospital Corps School course may request exemption. Requests for such waiver should have the commanding officer's endorsement thereon and should be addressed to the Chief of Naval Personnel via the Chief of the Bureau of Medicine and Surgery. (Personnel Div., BuMed)

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BuPers Designator Numbers for Warrant Officers of the Hospital Corps: The Officers Code Designator issued by the Chief of Naval Personnel lists the following:

Warrant Officers, Hospital Corps, (General)	8171
Warrant Officers, Hospital Corps, (Dental Clerk)	8172

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BUMED CIRCULAR LETTER 48-94 3 September 1948

To: All Shore Stations (except hospitals) having Medical and/or Dental Department Property

Subj: Statement of Receipts and Expenditures of Medical Department Property, NavMed-E; Instructions Regarding

Refs: (a) BuMed C/L 45-163 dated 30 June 1945
(b) BuMed C/L 47-92, AS&SL, July-Dec 1947, 47-685, p. 233
(c) BuMed C/L 47-166, AS&SL, July-Dec 1947, 47-1106, p. 253

This letter cancels reference (a). Paragraph 8 of reference (b) is modified to the extent that the gross amount of both Dental and Medical Departments shall not be recorded. The values of the materials of the Medical and Dental Department shall be reported separately. Instructions are contained for the preparation and submission of NavMed-E. (Revised 7-48). It will be noted that the Bureau desires only the original of this report.

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BUMED CIRCULAR LETTER 48-95 8 September 1948

To: Commandants Naval Districts (Except 10) and Potomac River Naval Command
Attn: District Director of Naval Reserve and Director of Training

Subj: First Aid Supplies and Biologicals for Naval Reserve Electronic Warfare Drill Quarters and Electronic Warfare Stations

Ref: (a) BuMed Cir. Ltr. No. 48-51 of 6 May 1948.

This letter (1) cancels and supersedes reference (a), (2) authorizes certain items for subject facilities, and (3) contains instructions for addressees concerning submission of NavMed-4 for required items, stock maintenance, and charge against the appropriation "Medical Department, Navy."

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BUMED CIRCULAR LETTER 48-96 9 September 1948

To: Naval Shore Stations (as per attached list)

Subj: Contract for Care of the Dead, Fiscal Year 1949

It is requested in this letter that addressees furnish BuMed with the name and address of the undertaker to whom the contract for care of the dead for the fiscal year 1949 has been awarded.

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BUMED CIRCULAR LETTER 48-97 9 September 1948

To: All Continental Naval Hospitals and Stations having Dispensaries

Subj: Immunizations for Dependents and Civilian Employees of Army and Air Force Prior to Movement Overseas

1. Dependents and civilian employees of the Armed Forces sometimes receive overseas travel orders while not living near a medical facility of the Department under whose cognizance they come.

2. When an Army or Air Force medical facility is not available, naval medical facilities shall provide, so far as practicable, the required basic immunizations for Army and Air Force dependents and civilian employees under orders for overseas travel. This is in accordance with reciprocal immunization service offered by the Army and the Air Force.

3. The orders issued to an individual, or a letter, from the Army or Air Force agency processing the individual for overseas travel contain detailed information as to the immunizations required; and may be accepted as identification at the naval medical facility, insofar as the request for immunization is concerned.

BuMed. H. L. Pugh

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BUMED CIRCULAR LETTER 48-98 13 September 1948

To: All Stations

Subj: Medical Training Films and Other Medical Audio and Visual Aids, Availability of and Report on

Refs: (a) BuMed CirLtr No. 48-17 of 12 Feb 1948; N.D. Bul. of 15 Feb 1948, 48-86.
(b) BuMed CirLtr No. 48-54 of 12 May 1948.

1. References (a) and (b) are hereby canceled. The letter report of medical training films and other medical audio and visual aids is no longer required and shall be discontinued immediately.

--BuMed. H. L. Pugh